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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,613	03/23/2004	Hong Liu	021288-002710US	4470
20350	7590	12/07/2006	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP			ANDERSON, REBECCA L	
TWO EMBARCADERO CENTER			ART UNIT	
EIGHTH FLOOR			PAPER NUMBER	
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DATE MAILED: 12/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/807,613	Applicant(s) LIU ET AL.	
	Examiner Rebecca L. Anderson	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) 2,3,5,6,10-15,21,22 and 29-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,7-9,16-20 and 23-28 is/are rejected.
- 7) ☒ Claim(s) 1,4,7-9,16-20 and 23-28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 August 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9/29/06, 2/14/05, 3/23/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-37 are currently pending in the instant application. Claims 1, 4, 7-9, 16-20 and 23-28 are objected and rejected. Claims 2, 3, 5, 6, 10-15, 21, 22 and 29-37 are withdrawn from consideration as being for non-elected subject matter.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-28 and the election of compound 218 in the reply filed on 29 September 2006 is acknowledged. The traversal is on the ground(s) that there is no burdensome search. This is not found persuasive because the inventions are independent and distinct because there is no patentable co-action between the groups and a reference anticipating one member will not render another obvious. Each group is directed to art recognized divergent subject matter which require different searching strategies for each group. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

The requirement is still deemed proper.

Therefore, based upon applicants' elected group and specific compound, as stated in the restriction requirement, **the elected invention for search and examination is:**

The products of the formulas as found in claim 9 and claim 18 wherein:

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R1 is a member selected from the group consisting of C6-C10 aryl substituted with 0-3 R1a or a C3-C8 cycloalkyl substituted with 0-2 R1b, wherein said C3-C8 cycloalkyl is saturated or unsaturated;

each **R1a** is independently a member selected from the group consisting of H, C1-C3 perfluoroalkyl, C3-C7 cycloalkyl, F, Cl, Br, CN, NO₂, OR₁₀, SCH₃, S(=O)CH₃, S(=O)₂R₁₀, NR₁₁R₁₂, acetyl, C(=O)OR₁₃, C(=O)NR₁₃R₁₄, S(=O)₂NR₁₃R₁₄, phenyl substituted with 0-3 R₁₅ and a C1-C4 alkyl substituted with 0-2 R₁₆;

each **R1b** is independently a member selected from the group consisting of H, OH, F, Cl, acetyl, =O, C1-C6 alkyl, C1-C6 alkoxy, CF₃ and OCF₃;

R2 is a member selected from the group consisting of a phenyl substituted with 0-3 R₁₅, a C1-C6 alkyl substituted with 0-2 R_{2a}, a C2-C6 alkenyl, a C2-C6 alkynyl, a C3-C7 cycloalkyl substituted with 0-2R₁₉, and a C7-C11 bicycloalkyl substituted with 0-2R₁₉;

each **R2a** is independently a member selected from the group consisting of a C6-C10 aryl substituted with 0-3 R₁₅ or a C3-C8 cycloalkyl substituted with 0-2R₁₉, and a C7-C11 bicycloalkyl substituted with 0-2 R₁₉;

R5 is a member selected from the group consisting of H, C3-C7 cycloalkyl, C2-C6 alkenyl, C2-C6 alkyne, phenyl substituted with 0-2R₁₅, or a C1-C6 alkyl substituted with 0-2R₁₈;

each **R10** is independently a member selected from the group consisting of H, C3-C7 cycloalkyl, a C1-C3 perfluoroalkyl, a C1-C4 alkyl substituted with 0-1 R₂₅, a phenyl substituted with 0-3 R₁₅;

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each **R11** is independently a member selected from the group consisting of H, tBOC, Cbz, C3-C8cycloalkyl, (C1-C6 alkyl)-C(=O)-, (C1-C6 alkyl)-S(=O)₂- and a C1-C6 alkyl;

each of **R12**, **R13**, and **R14** is independently a member selected from the group consisting of H and C1-C4 alkyl;

each **R15** is independently a member selected from the group consisting of H, OH, F, Cl, Br, I, CN, NO₂, COOR₁₃, C(=O)NR₁₃R₁₄, S(=O)₂NR₁₃R₁₄, acetyl, -SCH₃, -S(=O)CH₃, -S(=O)₂CH₃, NR₂₆R₂₇, C1-C6 alkoxy, C1-C3 perfluoroalkyl, C1-C3 perfluoroalkoxy and a C1-C6 alkyl;

each **R16** is independently a member selected from the group consisting of H, OH, COOR₁₃, C(=O)NR₁₃R₁₄, S(=O)₂NR₁₃R₁₄, acetyl, -SCH₃, S(=O)CH₃, S(=O)₂CH₃, C1-C6 alkoxy, NR₂₆R₂₇, a phenyl substituted with 0-3 R₁₅;

each **R18** is independently a member selected from the group consisting of H, OH, F, Cl, CN, NO₂, C(=O)OR₃₀, C(=O)NR₁₃R₁₄, NR₁₁R₁₂, a C1-C3 perfluoroalkyl, a C1-C3 perfluoroalkoxy, a phenyl substituted with 0-3R₁₅ and a C3-C8 cycloalkyl;

each **R19** is independently a member selected from the group consisting of C1-C4 alkyl, F, Cl, and C1-C4 alkoxy, CF₃ and OCF₃;

each **R25** is independently a member selected from the group consisting of H, C3-C7 cycloalkyl, a phenyl substituted with 0-3 R₁₅;

each **R26** is independently a member selected from the group consisting of H, C1-C4 alkyl, (C1-C4 alkyl)-C(=O) and (C1-C4 alkyl)-S(=O)₂;

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each **R27** is independently a member selected from the group consisting of H and C1-C4 alkyl;

each **R28** is independently a member selected from the group consisting of H, a C1-C6 alkyl, C3-C8 cycloalkyl, a phenyl substituted with 0-3 R15, a benzyl substituted with 0-2 R15;

each **R29** is independently a member selected from the group consisting of H, F, Cl, Br, I, CN, NO₂, OR₂₈, SR₂₈, S(=O)₂R₂₈, S(=O)₂NR₁₃R₁₄, NR₂₇R₂₇, acetyl, C(=O)NR₁₃R₁₄, C(=O)OR₁₃, C1-C6 alkyl, OCHF₂, SCF₃, OCF₃, -C(=NH)NH₂; and

each **R30** is independently a member selected from the group consisting of H, C3-C7 cycloalkyl, C1-C4 alkyl substituted with 0-1 R₂₅, a phenyl substituted with 0-3 R₁₅.

The remaining subject matter of claims 1, 4, 7-9, 16-20 and 23-28 that is not drawn to the above elected invention and the subject matter of claims 2, 3, 5, 6, 10-15, 21, 22 and 29-37 stands withdrawn under 37 CFR 1.142(b) as being for non elected subject matter. The remaining compounds which are not within the elected invention, which are independent and distinct from the elected invention and do not have unity with the species elected and therefore are withdrawn by means of a restriction requirement within the claim are, for example, the compounds wherein: R₁ is a 5 to 6 membered monocyclic or 8 to 10 membered bicyclic heteroaryl; R_{1a} is a 5 to 6 membered monocyclic heteroaryl; R₂ is a 5 to 6 membered monocyclic heteraryl; R_{2a} is a 5 to 6 membered monocyclic or 8 to 10 membered bicyclic heteraryl, R₅ is a 5 to 6 membered heteraryl, R₁₀ is a 5

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to 6 membered heteraryl, R16 is a 5 to 6 membered heteraryl; R18 is a 5 to 6 membered heteraryl, etc..

The above mentioned withdrawn compounds which are withdrawn from consideration as being for non elected subject matter differ materially in structure and composition from the compounds of the elected invention. The withdrawn compounds differ from those of the elected invention such as by, tetrazolyl, diazolyl, triazolyl, etc. which are chemically recognized to differ in structure and function. This recognized chemical diversity of the compounds can be seen by the various classification of these compounds in the U.S. classification system, i.e. class 548 subclass 250+ (tetrazolyl), class 548 subclass 300.1+ (diazolyl), class 548 subclass 262.2+ (triazolyl), etc. Therefore, again, the compounds which are withdrawn from consideration as being for non elected subject matter differ materially in structure and composition and have been restricted properly as a reference which anticipated but the elected subject matter would not even render obvious the non-elected subject matter. Nowhere do applicants argue to the contrary. Nowhere do applicants point out and give reasons why the claims do not involve independent or distinct subject matter. These withdrawn compounds are independent and distinct from the elected invention and do not have unity with the species elected and are therefore withdrawn by means of a restriction requirement within the claims.

Therefore, Applicants' traversal of the restriction requirement has been considered but is not found persuasive. Under 35 U.S.C. 121, the claims may be

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restricted and the examination limited to a restricted invention. Accordingly, restriction as has been presented in this application is proper.

Claim Objections

Claims 1, 4, 7-9, 16-20 and 23-28 are objected to as containing non-elected subject matter. Claims 1, 4, 7-9, 16-20 and 23-28 presented drawn solely to the elected invention as identified supra as the elected invention for search and examination would overcome this objection.

Claims 9, 18, 20 and 24 are objected to because of the following informalities: Claims 9, 18, 20 and 24 do not end in a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 7-9, 16-20 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds and pharmaceutically acceptable salts thereof, does not reasonably provide enablement for prodrugs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

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In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the elected invention is the compounds of the formulas as found in claim 9 and 18 and their pharmaceutically acceptable salts and prodrugs.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that prodrugs can be formed by various mechanisms and vary depending on the functional groups present in the parent compound, i.e. different prodrugs would arise from parent compounds containing varying functional groups, such as a carboxylic acid, an alcohol or an amine, all of which would require differing mechanisms.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is for the compounds of the formulas as found in claims 9 and 18 and their pharmaceutically acceptable salts. There is no data present in the instant specification for the preparation of prodrugs of the instant compounds of the elected invention. The paragraph on page 14 does not provide any examples or methods of preparation of prodrugs.

The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically, the instant claims include any covalently bonded compound that would release the active parent compound.

The quantity or experimentation needed and the level of skill in the art

While the level of the skill in the pharmaceutical arts is high, it would require undue experimentation of one of ordinary skill in the art to prepare any prodrug of the elected invention as instantly claimed since it would also require undue experimentation to prepare any covalently bonded compound that would release the active parent drug since prodrugs are formed by varying mechanisms and depend on the functional groups of the parent compound. The only guidance present in the instant specification is for the compounds of the elected invention and pharmaceutically acceptable salts thereof. There is no guidance or working examples present for prodrugs of the elected invention. Therefore, the claims lack enablement for all prodrugs of the compounds of the elected invention. This rejection can be overcome by deleting the phrase "or prodrug" from the instant claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 26 and 28 refer to tables in the specification. Claims must, under modern claim practice, stand alone to define an invention, and incorporation into claims by express reference to the specification is not permitted. *Ex parte Fressola*, 27 USPQ 2d 1608 (1993).

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

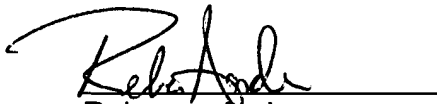
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public

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Rebecca Anderson
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Art Unit 1626, Group 1620
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December 1, 2006